Fluorescent probes for super-resolution imaging of protein aggregation

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In recent years, super-resolution microscopy has revolutionised the study of biological and synthetic nanostructures by breaking the diffraction limit, and allowing visualisation of cells and materials on the molecular scale.[1] While this Nobel Prize-winning technology demonstrates great potential for biomedical researchers wishing to unravel molecular-level interactions, the quantitative information obtainable and the progress in this field, is greatly limited by the limited number and poor photophysical properties of existing fluorophores.[2]

Protein misfolding and aggregation are hallmarks of many neurodegenerative diseases.[3] A key question in this field is the nature of the differences between globular and fibrillar aggregates of these proteins and how the histopathologic patterns relate to the different types of FTLD. Therefore, an ability to visualise the molecular-level organisation, structure and distribution of proteins in these proteinopathies is cardinal to gaining deeper understanding of the mechanisms underlying the associated neurodegeneration. As will be described in the presentation, we have developed a novel fluorescent sensor (AmyBlink) that utilises the amyloidophilic properties of the benzothiazole scaffold. AmyBlink-1 exhibits change in its emission profile: turn-on in fluorescence and blue-shifted emission maxima. In addition, AmyBlink-1 exhibits photoswitching properties allowing for super-resolution imaging of amyloid fibrils. These sensors are highly valuable tools to researchers working towards developing improved molecular tools for super-resolution imaging and understanding neurodegenerative pathologies.

References

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